Discussion of Next Steps, Work Plan and Final Work Studies
Facilitators: Huntington F. Willard, Ph.D. and Cynthia E. Berry, J.D.

DR. WILLARD: So we now have I guess 45 minutes for the committee to have a discussion to address next steps, to digest what we've heard today, and hopefully distill that down to what we've learned today and how that impacts the kind of issues we would like to tackle in a report which would be transmitted eventually to the Secretary.

I have some thoughts, but I think I'll hold those for the time being and simply see if other committee members want to start off a conversation. Debra?

DR. LEONARD: I'll start off being a little controversial. In listening to all the sessions we've had on large population studies, it seems to me that this project is much bigger than NHGRI or the NIH, and that right now it's coming from a science, even a genetics, perspective and could get into a lot of trouble. I'm concerned that NHGRI is not engaging the expertise or resources of the other relevant agencies -- CDC, AHRQ, HRSA, EPA, and other agencies that I don't even know the initials of who may be relevant to this project -- and I think that these agencies have a lot to contribute, if not being essential, to the success of the project.

So I was wondering if the other members of SACGHS were feeling the same way and maybe what we need to request is for something from the agencies as a group to come to us with a plan of how to better work together, rather than this having to be solely an NHGRI-driven initiative.

DR. KHOURY: Just to correct Debra, and I'm sure Francis will add to this, there have been several contributions from members of CDC for that report that you see.

I think the way I look at this is that right now, if we think about this as a research study that's going to involve 500,000 people to be collected on genes and environmental factors and be followed up over time, that's sort of one issue, and I think there has been a lot of thoughtful comments and discussion from the group that Francis assembled, which involves multiple agency representatives as well as the scientific community at large.

I think the implementation of where we want to go next, if we think of it as a national resource, then I think the advice that this group can give to the Department is about a study that's in the context of the general translation of genome science into population benefits, because this is the first time that we are embarking on a study that's beyond the test tube, beyond gene sequencing, and trying to figure out what genes mean for the health of people who live in Michigan or Hawaii or wherever, and then figure out how to use that information for prevention and treatment and medicine in general.

So I think as you all deliberate in your discussion here, think about the context. Think about not only a study in a particular time, but as part of an initiative that the various HHS agencies can rally around, because we all have slightly different missions, but other than NIH, we're all in one shape or form or some iteration into the process of translation, of translating the basic science that NIH sponsors and produces into population health benefits.

So we've heard, for example, throughout the day a lot of issues around the community engagement, the education of the public, the public policy issues, the ELSIs and, in a larger context, the involvement of state health departments and the convening power of public health, because at the end of the day, this is a public health research endeavor, because it purports to

generalize the finding of a series of studies under a big banner into what it means to the health of communities.

I mean, the whole Human Genome Project was done with the blood of one or two people or under 10. Here we're talking about basically a lot of people coming together.

So there are all these issues that will have to be weighed in and discussed by the committee as you produce your final report. As you said earlier, the report is not going to reflect the scientific merit of the study, but the broad policy and public implication of a study like this in the context of the current health system as we know it today.

One thing that I'm sure the committee does not want to end up with is by widening the gap between the research enterprise in genomics and the application enterprise in genomics because right now the gap is large in the sense that there is a lot of public and private resources going to discovering genes, both from NIH and the private sector, but very little in the context of translation, and if you want make a real impact, I think that view should be a little bit more balanced than providing advice on one study in one given point of time.

DR. WILLARD: I'm going to go to Francis just because it specifically deals with NIH.

DR. COLLINS: Briefly, again, I'd like to reassure Debra that there is no expectation at all that if a project of this sort were ever to actually get off the ground that it would be run by NHGRI.

This was sort of a difficult circumstance this morning. I found myself probably talking too much and defending the project in part because we didn't have in the room a lot of the people that were involved in that year-long study that had generated a lot of the study design considerations, most of whom were actually not from the government. They were scientists of various expertises in the extramural community.

NHGRI's role so far I think has been to be sort of a convener to try to get people to think about this and the scientific opportunity kinds of questions that come out of it, but if this were to get underway, it would never succeed without the full participation and a partnership of many of the government agencies that are represented around this table, and some that are not, like EPA, for instance.

Furthermore, I think there would need to be significant partnership opportunities explored with the private sector because it's the kind of data that they're also very interested in and potentially might be willing to help cover part of the cost.

So as far as, if it were to get off the ground, where would it be located, I have no idea. Would it be at NIH? Would it be somewhere else? If it was at NIH, would it be in one of the institutes that's used to doing large studies, like the Cancer Institute or Heart, Lung, and Blood Institute? Maybe. Would it be in the Director's Office? I have no idea. We're nowhere near the point of beginning to think about those issues.

DR. WILLARD: Kevin?

DR. FITZGERALD: I thank Francis for this because it was a great segue right into I think you're absolutely right, all those groups would have to be involved, but I think if there's one thing we heard that was at least clear to me today, if this goes anywhere, it has to have the public

engagement. This has no traction without the public. It is a public health issue. The public has to be on board.

I mean, we can leave it up to somebody else. We can leave it up to the Secretary to bring in more experts to decide exactly how to go about that, but I think if there's anything that we suggest along with this, the one thing we did hear clearly is not only does the public have to be engaged, it has to be engaged immediately and be part of the process all the way through.

The points that the bioethicists brought up, at least Hank and Pilar, is this feedback question. Well, if there's continual conversation with the public, I think in many ways that at least mitigates that issue to a significant extent. If we have structures in place to continually get feedback from this constructive engagement, then I think that helps certainly address a lot of those issues.

DR. WILLARD: Other comments? Jim?

DR. EVANS: Yes, I was just thinking that it would be helpful to get some data or get some expert opinion on the feasibility in the broadest sense, given the fact that we're talking about a prospective study of a huge number of people in an environment in which, I think Joann Boughman put it nicely, we have a very fractious health care system.

I know from personal experience that trying to keep up with people in a large study, much smaller than this, is extraordinarily problematic, and if we were in New Zealand, I think the question would be different and the question would be much easier, and I think it might be worth getting some expert advice about just the simple feasibility in a broad sense of this kind of thing in this country with our health care system and its balkanized nature.

DR. WILLARD: You could ask the IRS. They have experience in this country.

(Laughter.)

DR. EVANS: Yes, they can track people down pretty well.

DR. WILLARD: Debra?

DR. LEONARD: Jim and I were talking at one of the breaks and it does seem astounding how many things, issues, would be addressed and so much easier if there were a national health care plan. That doesn't seem within our purview to make comment on, but it's something that, having sat on this committee long enough and listened to SACGT also, it just keeps raising its head, and can we just ignore it? Or can we not ignore it, I guess, is my question?

DR. WILLARD: Well, we can certainly put anything in the report we wish to point out what may be obvious already to the Secretary that that makes it more difficult to mount a study like this in this country than in other countries. I don't think we can recommend to him that he change it suddenly, but we can certainly point that out.

DR. LICINIO: In that spirit, I'd like to ask Francis what's the difference, although obviously it's like two different countries, but in terms of what we propose to do, between this and DeCODE, with the commercial issues aside?

DR. COLLINS: Well, the commercial issue is a pretty significant one to set aside. Well, obviously it's a very different population. What you learn about the role of genes and

environment in Iceland may or may not map nicely across to somebody living in L.A. I think if we really want to understand those interactions, you need to apply across a broader and more heterogeneous group than what you're going to get from that somewhat exceptional part of the world, even though I'm sure a lot of very interesting things will come out of that.

But the other obvious one is the whole idea of data access. The intention of a U.S. study, as I think most of us have talked about it today, would be that this would be a data set that lots of people with ideas would have access to and they could intersect what you learn from environmental and clinical and genetic exposures with other kinds of data that are coming out of our advances in biology. That just empowers a much greater opportunity for things to be developed that are going to be useful and exciting.

Let me just say, I was a little worried about Jim's comment that we don't know how to do this. Again, I'm not an epidemiologist, but I've gotten to know a lot of them over the course of the last year and a half, and we do studies like this. Not at this scale, but look at the Multi-Ethnic Study of Atherosclerosis, for instance, MESA, following not anywhere near this number of people, but having all of those same problems and having pretty good success in terms of enrollment, in terms of ongoing participation and being able to do the follow-ups. Look at Jackson Heart. There are lots of experiences at NIH that make one believe it is possible to do this, although it's going to be hard.

DR. WILLARD: What's the scale difference, Francis, just for everyone's benefit?

DR. COLLINS: About a factor of 20.

DR. WILLARD: Kevin?

DR. FITZGERALD: Just to respond to what Debra was saying before, too, earlier in the day Francis pointed out that we might have some infrastructure challenges, but that pursuing a project like this could help one get the inertia to surmount some of those infrastructure challenges.

Similarly, engagement of the public, even just initially to just even think about the possibility of doing this, could also give you some inertia to address certain other particular infrastructure challenges, such as the lack of a non-fractured public health care system.

So many things could come out of this that would be good, not necessarily the specific ones that we're targeting, but again, that's the beauty of engaging the public.

Again, as I pointed out, too, in that one question that I asked and wanted everybody to be sure, also disappointments can come out of this. The public could say no. That's certainly a possibility. That's all part of the beauty of that kind of engagement.

DR. WILLARD: Joseph?

DR. TELFAIR: Sort of an observation and a question. If we look at the report, Hunt, that you did earlier about where we on the subcommittee agreed to stop and we look at what the nature of the discussion was today, that's kind of where we took off in the discussion. That's an observation.

So that means that do we go back, then, and reconsider that information in terms of should we begin to start talking more in detail about those things? Should we find another way to kind of

move forward with the things that we said to stop? I'm thinking in terms of next steps and a work plan, since that is what our charge is right now is to do, but I'm just observing that we did a lot of work. Granted, I should say the committee did, because I came in late to the committee, so I'll have to have truth in advertising, but it still seems to me that a lot of what was discussed today is sort of next steps.

DR. WILLARD: I think we have before us the opportunity to do whatever we'd like. I mean, we could, within the context of the prioritization process, decide that this was the only important issue we have left before us and that we should spend the next year addressing this issue. At the other extreme, we could stop now and simply say that after having spent two meetings' worth or parts of two meetings' worth being brought up to a certain level of knowledge and understanding and sensitization around certain issues that we're now ready to sit down and write up a report as we did on the reimbursement issue and share those thoughts that we have with the Secretary or anywhere in between.

So a good question to ask of the group now is are there particular issues that we either heard about today or didn't hear about today that we feel are so important that we need to hear about them again in some future meeting? Or do we feel that we actually have had a fairly good, broad discussion of many of the policy and process issues sufficient for us to then go ahead and say something intelligent, or hopefully intelligent, to the Secretary?

Sylvia, and then Joseph.

MS. AU: I think I would like to try to have a report, and this is going to be difficult, that simply describes the complexity of this project or this proposal with the recommendation that the only way to do this is with this community consultation process as the starting point to see how the public responds and what they want to do and how they want to do it. So I don't know if we can simply describe this complex project in just simple terms with that strong recommendation. I don't want to bog the report down in too many recommendations. I want the Secretary to realize how strongly we feel about community input.

DR. TELFAIR: I was actually going to say something similar, but actually a little bit more expanded than that, because it seemed to me that if we listen to everything that was talked about today, that there's a taking off point on a lot of these things. It seems to me that the more instructive thing to do is not only to talk about the issue of public engagement, which is a key issue, but in each one of these areas where people presented, to me there was a lot of commonality in what was being recommended.

It seems to me if we take that information and condense it into where we stopped and said here's what we understand about the key issues that we talked about, here are the common things that everyone's recommended, and here would be recommended next steps on how to address these things.

It may be that we as a committee cannot do that in a very short period of time. We may have to go back and do some more consultation or discussion on it, but in terms of being instructive and to really take this and make it a dynamic document that is actually practical and you can see that it has some legs to it, I think that one of the things to do would be to really think seriously and seriously review what has been told to us and come up with some real strong ways to really get it done.

That seems to me to make the most sense right now if we take everything we said today in terms of next steps. That would be my recommendation. That's kind of in the middle of what you're talking about, but I'm a person who's a bridger, so I always look for the middle, because I think the middle is very, very doable most of the time.

DR. WILLARD: Well, certainly one possibility, and either Amanda or Sarah or someone will tell me if I have the words wrong, but one option is to allow a small group, which I think is called a work group, which includes not only members of the committee, but also allows us to take advantage of some of the expertise from some of our panelists today, and do essentially what you said, to assume that our notetaking was insufficient in and of itself, so we might need some more expertise ongoing to help us draft the report as opposed to simply turning to poor Amanda and saying go to it and let us know when you're done.

Amanda's been great up until now, as we all know, those of us who were on the task force, but this would be a slightly more expanded way to drill down a little more deeply on some of the issues that we heard about today.

DR. TELFAIR: Well, I would recommend that if it's amenable to the group, because it seems to me that that's something very concrete we can do. I would recommend it to the committee. If the committee was amenable to that, it seems to me to make a lot of sense, and I would recommend that or put it on the table as a recommendation for where to go.

DR. WILLARD: Before opening this up to the full committee, let me just ask Sarah whether I have that right. Is that something that we have the option of doing and do we have to take any special action in order to do something like that?

MS. CARR: No, you can do that. In fact, I'm not sure, I think your task force could involve other people. So we could continue to call it a task force, but it would be governed by rules of working groups.

DR. WILLARD: So let me open it up. Suzanne?

DR. FEETHAM: In listening to the discussion, which was very profound and outstanding today as we've all acknowledged, but what I'm hearing now in the discussion of next steps is the reinforcement of the complexities and the challenges, and I think part of the discussion as we move forward in next steps is the potential of this and the rewards of this and why it's so significant to the potential health of the country over the next decades, and I think that should be part of our framework as the so what, and yes, we have to deal with all of the issues that were so eloquently presented today, but I think that's the context we need as we move forward with this.

DR. WILLARD: Muin?

DR. KHOURY: I think it might be quite useful, before we throw it back to the task force, of which I'm a member, to try to kind of have a general discussion, as we are having right now, to get the committee members to say -- I mean, to have sort of a roundtable to have the two or three top recommendations that if you were to address the HHS Secretary today, what would they be? Then the task force would take that in the context of all the stuff that we heard today and then digest it into some kind of a document, because at the end of the day, we know the complexities, but what we want is something that you guys will take our boss and tell him HHS should do A, B, and C, just like the way we took the reimbursement report, and then we can backtrack.

Now, if there are gaps or holes that would not allow us to make these kinds of at least draft recommendations, then we can go back to the committee or the task force and then rehash it a couple of times iteratively and come up with this.

But it would it be nice to get the members to say, okay, if I'm in the same room with the HHS Secretary today, what would I tell him around this issue?

DR. WILLARD: I would actually back up. There are two issues I'd like to go around to committee members and get everyone to comment on, and that would be one of them. What are the two or three leading issues that everyone can identify based on what they've heard and read?

But I think before I got to that, I think it's necessary to get a sense of the committee on level of enthusiasm, because there are actually many, many ways to write the report, but there are two sides to it. One is simply to throw the hands up and simply tell the Secretary and say this is the most complex thing I could ever imagine and you're going to have to reinvent the U.S. government system and the health care system, and God bless you.

(Laughter.)

DR. WILLARD: But good luck to you because this is an incredibly complicated issue, and by the way, here are some of the processes and mechanisms we think you may want to consider.

The other is to come at it -- and again, there's plenty of ground in the middle, so I'm overstating both extremes here for purpose. The opposite is to frame it the way I believe Suzanne was suggesting, which is to make sure that we're pointing out that there's a tremendous upside if we could figure a way to do it. If he could figure a way to do it, there's a tremendous upside here, and that we as a committee are very enthusiastic about it, or change the "very" word depending on each of our own feelings.

In order to give him that sense of recommendation, I don't think we necessarily need to either put our stamp of approval on this or not, but we could, and that depends in large measure on the sense of the group and on the level of enthusiasm for this before we then would necessarily go and identify the issues. I think it would help the writers of the report bring a report back to this committee, which is likely to be representative of the entire group.

So I'd like to go around and get a sense, and we don't need long speeches here, but we do need some sense of the committee members on a level of enthusiasm and level of feasibility to this whole challenge and whether this is something that we should urge the HHS Secretary to take on as a matter of some priority or whether this is something we're a little less enthusiastic about because of its extraordinary complexity and because of the depth of the issues that have already been identified.

So I'm looking on both sides, but since my body is turned in Joseph's direction, we'll start at your end, Joseph, and work our way around.

DR. TELFAIR: I would agree with Debra that it's a very complex proposal and body of work, but at the same time, it seems to me that we've looked through a lot of the issues around it, and I think with a little bit more review, I would be able to make a real decision. I'm highly enthused about looking a little bit more deeper at some of the more complex issues in terms of feasibility. That's what I would be enthused about, is to see that, because I think that the study itself has significant merit, but I recognize there are limitations. So that's where my vote would be.

DR. WILLARD: Jim?

DR. EVANS: There's no question in my mind that such a study would be very interesting and give us important information. My biggest hesitation is not that. It's trying to balance that with the obvious incredible complexities of such a study, especially in the kind of environment we find ourselves in with the U.S. health system.

I think that perhaps to me the most interesting question remains can we get these kinds of data and can we derive most of the benefit of such a study through the types of case/control studies and the types of population studies, albeit more limited and focused, that are currently going on?

Talking about kind of doing the whole nine yards with really rich phenotypic data, with long prospective follow-up, I'm not sure that the information we get is going to necessarily be of orders of magnitude more value than what we can get from smaller studies, but we can certainly be assured that the complexity and cost will be very great.

So to me, the big question is not would this turn out important things? It would. It's could we get most of that information through the types of studies that are going on now and that are going on in other countries? That's the big question, and what we have to decide is would we recommend to do this with various recommendations around that or would we recommend a more limited type of focus. That's kind of my inchoate thoughts at this time, but I think we need to discuss it.

DR. WILLARD: Chira?

MS. CHEN: I'm not as negative about this. I think it's pretty innovative, and with the talk from Yvonne Lewis, I was very surprised about how engaged the public is willing to accept this, and if we could get the public involved and get that first step to recruit the people and let them understand this, we probably will be able to use that as a push to form policy issues, to have all the other stuff to put together to get this thing working.

So from that point of view, it is a very complex project and it's going to be a very expensive project, but with the help of the public, we probably will be able to work it out somehow.

DR. WILLARD: Kevin?

DR. FITZGERALD: I actually am reveling in the complexity and the challenge of this project because I think it in and of itself may be, and I'm trying to think of any other examples I could think of, but it may be right now the best opportunity we have because this is kind of new, so it's not politically entrenched. It's not gridlocked anywhere, though it may become that way once we get the public involved, so you have to ask Muin and Francis if they want to die in this trench.

(Laughter.)

DR. FITZGERALD: But here is a possibility of bringing something to the public that is right now not polarized or gridlocked, so that we could use this to get public engagement going and perhaps set a precedent, at least set a precedent, that way because this is in one sense no more complex or costly or anything than a lot of the other stuff that's coming down the pike that the U.S. public is going to have to face.

So if we can find a starting point -- and I don't know. I'm just trying to think if there's a better one, but I like this one, not in the sense that I think it's necessarily going to work, but I think it's a great starting place for that kind of public engagement and discussion to see if it could.

DR. WILLARD: Agnes?

MS. MASNY: Well, I agree with everyone regarding the complexity of the project, but I fall back on what we were assigned to do in our charter is actually from the Secretary's Advisory Committee to actually look at the impact of the Human Genome Project on all the aspects of health, society, and medicine, and I think that if we don't support or fail to support a way that we could conduct this large population study, we will fail the charter that we were given to do.

So I think that from that perspective, that is one of the main reasons why we should move ahead in whatever fashion we take, whether we have to look further at some of the issues before we put recommendations forward. I think it is well worth and I enthusiastically support moving forward with recommending this to the Secretary.

You had asked also, Hunt, regarding some of the other key issues, and I think just to reiterate what people had said about the issue of community involvement and community engagement, one of the things that we would need to look at would be actually developing a whole new paradigm for the way research would be conducted with this aspect of community engagement. I know the CDC has a whole network of CDC Community Partnerships for Prevention, and we would have to look at both the national level of engagement of community partners as well as local levels, and maybe that would be one thing that we would need to look at a little further in terms of making our recommendations.

DR. WILLARD: Cindy?

MS. BERRY: In all of the comments that I heard today, I didn't hear that this was not a worthwhile endeavor. I heard that there are some complexities and there are timing issues and cost issues and things that we need to be mindful of.

So I'm in the category of the enthusiastic supporters for the concept. I mean, it's like going to the moon. I think others perhaps have used that example, and I see no reason why we can't think big and embrace the idea and regard our job as helping to guide the Secretary and helping guide the process so that we're on the right course. I think it's really more a matter of timing and making sure that things are lined up and everyone is thoughtful about it.

So I'm in the category of enthusiastic yeses and I think our report or our job should be in helping to figure out how we get there and over what period of time and addressing all of the different issues that were raised.

DR. WILLARD: Julio?

DR. LICINIO: From my own perspective, I see this potential study as both revolutionary and visionary, and I think it would give power that does not exist in current studies.

For example, I study depression, which, surprisingly enough, clinically relevant depression has a rate of 15 percent in the population. So if you study 500,000 people, you would have 75,000 people with depression who would be genotyped and that we know their phenotype and environment. That doesn't exist anywhere in the country. It would be a unique resource.

For obesity, the lowest rate I can think of is 30 percent. So that would be 150,000 people genotyped with obesity, and there is no way that (unclear word) is going to go out and genotype and categorize 150,000 people with obesity.

So the difficulty I think is that given its unprecedented scope, we could talk about it forever and never get it done, so we have to decide when do we stop talking about it and begin it, which I think would be a key issue for the Secretary.

But then, on the other hand, we do not also want to kind of begin the project with built-in structural flaws that we're not voicing ahead of time. So a suggestion that I would make would be to define timelines for key elements and stick to it, and importantly I think give the Secretary kind of a suggestion that maybe we should decide what things need to be decided a priori and address those in a thoughtful way, but time-limited, and then go ahead and do it.

Then also, define other issues that could be decided as the project goes along, and then set milestones for those maybe, let's say, every year, and then set up new things -- you know, you don't predict everything that's going to happen before you do it -- and set deadlines for those.

But I think we should neither try to talk about it to death nor start without a thoughtful process. Those two things have to be very well balanced.

DR. WILLARD: Debra?

DR. LEONARD: Well, I'm in the yes camp. This is a complex project, but I think from the beginning we've decided that the U.S. has a unique population by the heterogeneity of it, we can't use other population cohorts, and we're behind other countries. We were a leader in the Human Genome Project, so it seems sort of sad that we're lagging behind other initiatives like this.

I do think we should emphasize that it will require broad government agency and private sector involvement and participation.

I think that there has to be a public engagement mandate starting at the beginning, now, as soon as possible, as feasible, and emphasize that while there are hurdles, the potential benefits for individual and public health are enormous with the additional potential for other non-health outcomes that are not the focus of this project, like happened with the space initiative. I think there will be other outcomes of interest in science among young people and other kinds of things that will come out of this initiative if the public truly is engaged.

Can I add one other comment? Which is I was struck by Dr. Duster's point about the taxonomy that's being chosen for the representativeness of the cohort, and I would ask to consider something like a zip code taxonomy or something. I know there are billions of zip codes, but it just seems that you're basing a lot on race/ethnicity, and I think there's a real danger in that, having heard what Dr. Duster said. I think that's overemphasized. If it truly is a gene/environment study, then you need an environment taxonomy of some sort that's not in this study currently. I mean, as the work group proposed it.

DR. WILLARD: And Sylvia?

MS. AU: Well, I think that I'm very enthusiastic about this project because the rewards will be probably be more than going to the moon.

I think that this also gives us an extremely great opportunity to show how research can be done right in a large population if we do it right from the beginning. Of course, as I said, I'm really supportive of the community participation from the beginning.

I think that we have to emphasize that this needs to be new funding. We don't have enough funding right now for the research that is being done. It's being cut all the time. We need to have new funding for this.

Finally, that the participants need protections, protections from discrimination, protection from not receiving the proper health care. I don't want the situation that Julio was saying about watching people get sick. That is not acceptable to me. So if you're going to participate in the project, those participants need to have health care.

DR. WILLARD: Great. That was certainly useful to me, I think. My sense is -- and I'm watching the clock, so whatever we do, we're going to do it in the next four minutes. I see Muin and Joseph, and then I'm going to try to offer some final comments.

Muin?

DR. KHOURY: I'm not supposed to give my level of enthusiasm to such a study because I'm the ex officio here, but I wanted to react to a couple of things, one of them what Jim said, because you're the only one who brought the idea of could we do it through some other means. I think it's very important to at least give advice to the Secretary as we move to implement this initiative -- and again, four people here on what I heard keep saying this is a study. I heard one, two, three, four. You know, it's not a study. It's sort of a big initiative, but it's very important to have what I call the knowledge integration piece, sort of what are we learning from the existing cohorts, what have we learned from the existing case/control studies, what are we learning from the biobanks that are moving forward, and then figure out a way to integrate that knowledge as we move forward.

I mean, this is not as trivial as some people think, because pooled analyses and meta-analyses are a very complex thing. When I presented to the committee I think a couple of meetings ago about what HuGENet is doing, the Human Genome Epidemiology Network, as a matter of fact, last week, we just had a meeting in the U.K., Cambridge, where we brought together 24 networks from around the world that are primarily disease-based. Half of them are cancer. Osteoporosis, heart disease, Parkinson's, et cetera. These are consortia that have already existed for the last anywhere from five to 20 years. NCI and others have kind of nurtured them, and from the European Union, and that have collected thousands of cases and controls on specific disease topics. They have pooled analyses and DNA and they're working together to integrate their knowledge about genetic variation and that specific disease. There are other cohort studies, like ERIC and Framingham and the Women's Health Study and the Nurses' Study and the Physicians' Study.

So I think it's very important, at least from my perspective, to put in the advice that as we embark on this new endeavor or new initiative, that we need to provide enough resources for that knowledge integration from all the existing studies, whether they're case/control cohorts or biobanks that are beginning to be launched. Otherwise, we may be sort of missing the boat here and we may be studying things that we don't need to study because some other people have solved that question. So knowledge integration is the key.

DR. WILLARD: And Joseph?

DR. TELFAIR: Mine is brief. Hunt, if you can just answer also your perspective as you asked us to, I'd be curious.

DR. WILLARD: And I thought I was going to follow Reed and reserve the right not to say anything.

(Laughter.)

DR. WILLARD: No, I'm very enthusiastic about this. I'm full of question marks, but I think everyone who has dreamt about this study is full of question marks on how exactly to proceed.

I think for me the two issues are public engagement and how you do that and how early do you do it, and then, two, how one might creatively look at the issue of smaller starting studies, because you can't start on day one saying we want 500,000 samples and we're off to the races. So where can one get information earlier from a smaller set to teach us how to do this project as we go along?

The Human Genome Sequencing Project did exactly that. That's why some of the model organisms were done. There was a learning curve, and I think I'd want to think about ways in which that could actually be built into the process, so that we could learn from our mistakes and avoid them the second time and see what some of the gaps are, which we can't even anticipate now.

But I'm quite enthusiastic about this, despite the levels of complexity and despite an awful lot of what ifs that would have to be addressed by the Secretary.

DR. EVANS: As the one person who is probably perceived as the biggest wet blanket --

(Laughter.)

DR. EVANS: -- my plea would be that we do exactly what Muin has suggested. We need to learn as much as possible from the kinds of studies that have gone on and are going on already so we don't reinvent the wheel and so that we do this right.

DR. WILLARD: So with that, my sense of the committee is that the committee at large would like the task force to work with Amanda and staff to begin to draft a report, draft an outline, which the task force can be iteratively examining, and we can pull in other expertise as we see fit based on what we heard today, and then hopefully bring that back to the full committee as a draft document.

It's hard to answer by when without turning this way to -- I think it's impossible to say by when until we actually begin.

MS. CARR: Well, it's helpful to have some sense of that.

DR. WILLARD: I don't see how this could happen before the March meeting, which is the next one, right?

MS. CARR: That was what I was wondering about. Not beyond that.

DR. WILLARD: No.

Is there a sense of the committee that that's a reasonable series of steps? Then it would come back to the committee in order to both vet the report and identify issues that need to be drilled down a little more completely in that.

Francis, you had a point or a question.

DR. COLLINS: Just I would like to know, would the committee in the meantime encourage further exploration of how to conduct the public engagement? Because it sounded as if that was pretty broadly endorsed and I would hate to lose the time between now and March to begin to try to put something more concrete together along that line if you all believe that that's critical.

DR. WILLARD: Are you asking for a sort of preliminary note to the Secretary along those lines?

DR. COLLINS: I don't know if you have to turn it into a note to the Secretary, but just a sense of the committee that would justify perhaps NIH spending some money on this and not feeling as if we're completely out there on the limb.

DR. WILLARD: I would think you have the sense of the committee that this is a high-priority item that no one knows how to tackle and any efforts to learn more about how to tackle it would be welcomed.

With that, I would thank everyone for hanging through to the end. We'll reconvene tomorrow at 8:30 in the morning, and members of the committee planning to attend the dinner this evening, you should meet in the lobby at 6:40.

With that, thank you all.

(Whereupon, at 6:05 p.m., the meeting was recessed, to reconvene at 8:30 a.m. on Thursday, October 20, 2005.)